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L1: Entry 1 of 1

File: DWPI

Jun 18, 2002

DERWENT-ACC-NO: 2002-537532

DERWENT-WEEK: 200262

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TITLE: Novel dominant negative mutant sequence or constitutively active mutant sequence of Myo/V1 polypeptide, useful for treating cardiovascular disorders and inhibiting formation of NFkappaB homodimers

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PRIORITY-DATA: 2000US-243985P (October 27, 2000)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 200239777 A	June 18, 2002		000	A61K000/00
WO 200245659 A2	June 13, 2002	E	217	A61K000/00

INT-CL (IPC): A61 K 0/00

ABSTRACTED-PUB-NO: WO 200245659A

BASIC-ABSTRACT:

NOVELTY - A dominant negative mutant sequence (Ia) of Myo/V1 polypeptide (MP), or a constitutively active mutant sequence (Ib) of MP, as a composition of matter, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a nucleic acid sequence (II) encoding (Ia) or (Ib);

(2) screening (M1) a test compound (TC) for the treatment of cardiovascular disease, for anti-aging activity and for nuclear factor (NF)kappaB p50 polypeptide interaction, by combining a labeled nucleic acid sequence with a NFkappaB p50 subunit polypeptide under conditions to form a nucleic acid sequence-NFkappaB p50 polypeptide complex, adding TC to the complex, assaying the electrophoretic mobility (EM) of the complex in the presence of TC, comparing EM of the complex in the presence of TC to EM of the complex in the absence of TC, where a change in the mobility in the presence of TC indicates TC is an active compound;

(3) screening (M2) for an active compound for cardiovascular disease or anti-aging treatment, by introducing into a cell, a first nucleic acid expressing a fused test peptide/DNA binding domain, and a second nucleic acid expressing a fused Myo/V1-p50 polypeptide/DNA activation domain, and assaying for an interaction between the test peptide and the Myo/V1-p50 polypeptide by measuring binding between the DNA binding domain and the DNA activation domain, where the interaction between the test peptide and the Myo/V1-p50 polypeptide indicates the test peptide is the active compound;

(4) identifying (M3) an active compound for treating of cardiovascular disease or for the anti-aging treatment, by forming a Myo/V1-NFkappaB p50 complex in a cell, where the complex formation generates a detectable signal, adding a test compound to the complex in the cell under conditions where the compound interacts with the complex, and measuring a change is the visualizable signal, where the change indicates the test compound is the active compound;

- (5) a pharmaceutical composition (PC) for treating cardiovascular disease or for anti-aging treatment, comprising an active compound obtained by M1, M2 or M3;
- (6) treating cardiovascular disease or reducing NFkappaB p50 homodimer levels or NFkappaB p65 homodimer levels, in a cell of a mammal, by introducing NFkappaB repressor sequence into a cell of the mammal under conditions where the repressor sequence binds a NFkappaB p50 homodimer or NFkappaB p65 homodimer;
- (7) treating (M4) cardiovascular disease in a mammal, inhibiting formation of NFkappaB p50 homodimers in a cell of a mammal, or reducing formation of NFkappaB p50 homodimers in a cell of a mammal, by introducing a dominant negative mutant sequence (III) of a NFkappaB p50 subunit, or a nucleic acid sequence encoding (III), where (III) comprises a sequence given in the specification;
- (8) diagnosing (M5) cardiovascular disease in a mammal, by obtaining a sample from the mammal and measuring the level of NFkappaB p50 homodimers in the sample, where an increase in the level is indicative of the cardiovascular disease in the mammal;
- (9) reducing or preventing (M6) inhibition of expression of an adrenergic system signaling nucleic acid sequence in a cell of a mammal, by reducing the levels of NFkappaB p50 homodimers in the cell;
- (10) treating cardiovascular disease in a mammal, or reducing NFkappaB p50 homodimers in a cell of a mammal, by reducing migration of NFkappaB p50 homodimers from cytoplasm to nucleus in the cell of a mammal;
- (11) reducing Myo/V1-p50 complex levels in a cell of a mammal, by introducing ER81 or ETS factor polypeptide into the cell;
- (12) reducing (M7) levels of Myo/V1, NFkappaB p50 subunit, beta -adrenergic receptor kinase 1 (beta -ARK1) or beta -adrenergic receptor kinase 2 (beta -ARK2) in a cell of mammal, by introducing an antisense peptide nucleic acid (PNA) of Myo/V1, NFkappaB p50 subunit, beta -ARK1 or beta -ARK2 into the cell;
- (13) treating cardiovascular disease in a mammal, by administering antisense sequence of Myo/V1 or NFkappaB p50, to the mammal;
- (14) an aptamer which binds Myo/V1 or NFkappaB p50 polypeptide, as a composition of matter;
- (15) generating a nucleic acid aptamer or peptide aptamer for binding Myo/V1 polypeptide or NFkappaB p50 polypeptide; and
- (16) inhibiting fetal carnitine palmitoyltransferase-I (CPT1) nucleic acid expression or 6-phosphofructo-2-kinase/fructose-2, 6-bisphosphatase (PFK) nucleic acid expression in a mammal, by inhibiting interaction of Myo/V1 polypeptide with an ETS factor.

ACTIVITY - Cardiant; Vasotropic; Immunosuppressive; Vulnerary.

MECHANISM OF ACTION - Inhibitor of formation of NFkappaB p50 or NFkappaB p65 homodimers (claimed). No supporting data given.

USE - (Ia) or (II) is useful for treating cardiovascular disease including cardiac hypertrophy, myocardial infarction, ischemia/reperfusion injury and heart transplantation, in a mammal, for anti-aging treatment, for inhibiting formation of NFkappaB p50 homodimers or NFkappaB p65 homodimers in a cell of a mammal and for reducing formation of NFkappaB p65 homodimers in a cell of a mammal. M4 is useful for treating cardiovascular disease in a mammal. Active compound identified by M1 is useful for treating a NFkappaB-related disease (claimed).

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	RMC	Draw Desc	Image
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Terms	Documents
(aptamer or nucleic adj2 ligand) with NFkappaB	1

Display Format:

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L17: Entry 3 of 3

File: USPT

Mar 9, 1999

DOCUMENT-IDENTIFIER: US 5879917 A

TITLE: Programmable genotoxic agents and uses therefor

Detailed Description Text (36):

An important class of nucleic acid second agents 9 includes those known in the art as "aptamers". Aptamers are the products of directed, also known as in vitro, molecular evolution. The term "aptamer" was originally coined by Ellington and Szostak to describe the RNA products of directed molecular evolution, a process in which a nucleic acid molecule that binds with high affinity to a desired ligand is isolated from large library of random DNA sequences (Ellington and Szostak (1990), 346 Nature 818-822). The process involves performing several tandem iterations of affinity separation, e.g., using a solid support to which the desired ligand is bound, followed by polymerase chain reaction (PCR) to amplify ligand-eluted nucleic acids. Each round of affinity separation thus enriches the nucleic acid population for molecules that successfully bind the desired ligand. In this manner, Ellington and Szostak "educated" an initially random pool of RNAs to yield aptamers that specifically bound organic dye molecules such as Cibacron Blue (Id. at FIG. 2). Certain of the aptamers obtained could discriminate between Cibacron Blue and other dyes of similar structure, demonstrating specificity of the technique. Aptamers can even be engineered to distinguish between stereoisomers that differ only by optical rotation at a single chiral center (Famulok and Szostak (1992), 114 I. Am. Chem. Soc. 3990-3991). Originally, it was thought that RNA aptamers would be more suitable for ligand recognition, in view of established knowledge of naturally occurring RNAs with higher ordered three-dimensional structures (e.g., rRNA or transfer RNA, tRNA). However, single-stranded DNA molecules produced by asymmetric PCR amplification were also shown to be effective (Ellington and Szostak (1992), 355 Nature 850-852). It should be noted that aptamers can be prepared from nucleotide analogs, such as phosphorothioate nucleotides, which can offer increased aptamer stability under physiological conditions. Standard techniques are available for linking nucleic acids, such as transcription factor decoys and aptamers, to other chemical moieties, such as genotoxic drugs, without substantial loss of protein-recognition capability and genotoxicity.

C91425, 804

WEST Search History

DATE: Monday, March 10, 2003

Set Name Query

side by side

Hit Count Set Name

result set

DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR

L19	dithiophosphate same transcription adj2 factor	0	L19
L18	L15 not l17	24	L18
L17	L15 same transcription adj2 factor	3	L17
L16	L15 with transcription adj2 factor	0	L16
L15	phosphorothioate with (aptamer or nucleic adj2 ligand)	27	L15
L14	L13 with (aptamer or ligand)	3	L14
L13	decoy with transcription adj factor	76	L13
L12	decoy with NFkappaB	0	L12
L11	(rna or dna or nucleic) adj2 decoy with NFkappaB	0	L11
L10	L5 same inflam\$7	0	L10
L9	l6 with inflam\$7	0	L9
L8	l5 and l4	0	L8
L7	L4 not l5	22	L7
L6	L5 not l4	38	L6
L5	(aptamer or nucleic adj2 ligand) with transcription adj factor	38	L5
L4	(aptamer or nucleic adj2 ligand) with inflam\$7	22	L4
L3	ligand with NFkappaB	6	L3
L2	(aptamer or nucleic adj2 ligand) with NF adj kappaB	0	L2
L1	(aptamer or nucleic adj2 ligand) with NFkappaB	1	L1

END OF SEARCH HISTORY

WEST Search History

DATE: Monday, March 10, 2003

Set Name Query

side by side

Hit Count Set Name

result set

DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=OR

L14	L13 with (aptamer or ligand)	3	L14
L13	decoy with transcription adj factor	76	L13
L12	decoy with NFkappaB	0	L12
L11	(rna or dna or nucleic) adj2 decoy with NFkappaB	0	L11
L10	L5 same inflam\$7	0	L10
L9	l6 with inflam\$7	0	L9
L8	l5 and l4	0	L8
L7	L4 not l5	22	L7
L6	L5 not l4	38	L6
L5	(aptamer or nucleic adj2 ligand) with transcription adj factor	38	L5
L4	(aptamer or nucleic adj2 ligand) with inflam\$7	22	L4
L3	ligand with NFkappaB	6	L3
L2	(aptamer or nucleic adj2 ligand) with NF adj kappaB	0	L2
L1	(aptamer or nucleic adj2 ligand) with NFkappaB	1	L1

END OF SEARCH HISTORY

Zitomer, Stephanie

12-10-02

To: STIC-Biotech/ChemLib
Subject: 09/425,804

Please search SEQ ID NO:39 including interference search.

Thanks -

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